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J. VOGEL et al.

U.S. Application No.: 09/528,989

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For: INJECTABLE AND SWELLABLE MICROSPHERES FOR TISSUE BULKING

Attorney Docket No.: 9676-292-999

Name or type of paper being transmitted: **Pending claims in Application Nos. 09/528,991; 10/220,984; 10/220,982; 10/029,294; and 10/222,819 as requested.**

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PENDING CLAIMS

U.S. Patent Application No. 09/528,991, filed 3/20/00 (Our Ref.: 9676-293-999):

1. A method for dermal augmentation in a mammal comprising injecting a composition of elastic, hydrophilic, non-toxic and substantially spherical microspheres in a biocompatible carrier to said mammal through a needle of about 30 gauge or smaller; wherein the microspheres comprise a positive charge.

2. The method of claim 1, wherein the composition is a suspension of said microspheres in said biocompatible carrier.

3. The method of claim 1, wherein there is no aggregation or clumping of the microspheres prior to or during the administration.

4. The method of claim 1, wherein the microspheres comprise one or more elastomers.

5. The method of claim 4, wherein the elastomers are selected from the group consisting of acrylic polymers, acrylamide polymers, vinyl alcohol polymers, acrylate polymers, polysaccharides, silicones, or derivatives and mixtures thereof.

6. The method of claim 1, wherein the composition further comprises therapeutic agent, radio-pacifying agent, contrast media, or mixtures thereof.

7. The method of claim 6, wherein said therapeutic agents are bound to the microspheres.

8. The method of claim 1, wherein the microspheres are capable of being chemically modified to have therapeutic effects, anti-inflammatory effects, anti-bacterial effects, anti-histamine effects, or combinations thereof.

9. The method of claim 8, wherein the chemical modification of the microspheres are caused by interactions between the microspheres and neighboring tissues after administration thereof.

10. The method of claim 1, wherein the administration comprises injecting said composition into an area of said mammal in need of dermal augmentation.

11. The method of claim 10, wherein the administration comprises injecting said composition into the subcutaneous layer .

12. The method of claim 1, wherein the dermal augmentation is for treatment of contour deficiencies of said mammal.

13. The method of claim 12, wherein the contour deficiencies are caused by aging, environmental exposure, weight loss, child bearing, surgery, disease, or combinations thereof.

14. The method of claim 13, wherein the disease is acne, skin cancer, or combination thereof.

15. The method of claim 13, wherein the contour deficiencies are one or more of the group consisting of frown lines, worry lines, wrinkles, crow's feet, marionette lines, stretch marks, and internal or external scars resulted from injury, wound, surgery, bites, cuts, or accident.

16. The method of claim 1, wherein the mammal is human.

17. The method of claim 1, wherein the administration comprises injecting said composition extracorporeally into organs, components of organs, or tissues prior to their inclusion into said mammal's body, organs, or components of organs.

18. A kit for performing dermal augmentation comprising:

(a) a 30 gauge or smaller needle;

(b) means for injecting a liquid based composition through said needle; and

(c) biocompatible, elastic, hydrophilic, non-toxic and substantially spherical microspheres injectable through said needle and are not capable of being eliminated by macrophage or other elements of said mammal's immune system after injection thereof, wherein the microspheres comprise a positive charge.

19. The kit of claim 18, wherein the means for injection is a syringe corresponding to said needle.

20. The kit of claim 18, further comprising a liquid based biocompatible carrier injectable through said needle.

21. The kit of claim 20, wherein the microspheres are suspended in the biocompatible carrier.

22. The kit of claim 21, wherein the microspheres are associated with cells.

23. A method of tissue bulking in a mammal comprising injecting a composition of elastic, hydrophilic, non-toxic and substantially spherical microspheres in a biocompatible carrier to said mammal through a needle of about 18 to about 26 gauge; wherein the microspheres comprise a positive charge.

24. The method of claim 23, wherein the composition is a suspension of said microspheres in said biocompatible carrier.

25. The method of claim 23, wherein there is no aggregation or clumping of the microspheres prior to or during the administration.

26. The method of claim 23, wherein the microspheres comprise one or more elastomers.

27. The method of claim 26, wherein the elastomers are selected from the group consisting of acrylic polymers, acrylamide polymers, vinyl alcohol polymers, acrylate polymers, polysaccharides, silicones, or derivatives and mixtures thereof.

28. The method of claim 23, wherein the composition further comprises therapeutic agent, radio-pacifying agent, contrast media, or mixtures thereof.

29. The method of claim 28, wherein said therapeutic agents are bound to the microspheres.

30. The method of claim 23, wherein the microspheres are capable of being chemically modified to have therapeutic effects, vascularization effects, anti-vascularization effects, visualization properties, anti-inflammatory effects, anti-bacterial effects, anti-histamine effects, or combinations thereof.

31. The method of claim 30, wherein the chemical modification of the microspheres are caused by interactions between the microspheres and neighboring tissues after administration thereof.

32. The method of claim 23, wherein the administration comprises injecting said composition into an area of said mammal in need of tissue bulking.

33. The method of claim 32, wherein the injection is into the vocal cord.

34. The method of claim 23, the tissue bulking is for the treatment of gastroesophageal reflux disease.

35. The method of claim 34, wherein the administration comprises injecting said composition into the lower esophageal sphincter or the diaphragm of said mammal.

36. The method of claim 23, wherein the tissue bulking is for the treatment of urinary incontinence or urinary reflux disease.

37. The method of claim 36, wherein the administration comprises injecting said composition into the bladder sphincter or urethra of said mammal.

38. The method of claim 36, wherein the urinary incontinence is caused by bladder-neck hypermobility.

39. The method of claim 23, wherein the mammal is a human.

40. The method of claim 23, wherein the administration comprises injecting said composition extracorporeally into organs, components of organs, or tissues prior to their inclusion into said mammal's body, organs, or components of organs.

41. A kit for performing tissue bulking comprising:

(a) an 18 to 26 gauge needle;

(b) means for injecting a liquid based composition through said needle; and

(c) biocompatible, elastic, hydrophilic, non-toxic and substantially spherical microspheres injectable through said needle and are not capable of being digested or eliminated by macrophage or other elements of said mammal's immune or lymphatic system after injection thereof, wherein the microspheres comprise a positive charge.

42. The kit of claim 41, wherein the means for injection is a syringe corresponding to said needle.

43. The kit of claim 41, further comprising a liquid based biocompatible carrier injectable through said needle.

44. The kit of claim 41, wherein the microspheres are suspended in the biocompatible carrier.

45. The kit of claim 44, wherein the microspheres are associated with cells.

46. The method of claim 1, wherein the microspheres comprise a hydrophilic acrylic copolymer which comprises in copolymerized form about 25% to about 98% of neutral hydrophilic acrylic monomer by weigh, about 2% to about 50% of difunction monomer by weight, and about 0 to about 50% of one or more monomers having a cationic charge.

47. The method of claim 1, wherein the microspheres further comprise a cell adhesion promoter.

48. The method of claim 1, wherein the microspheres further comprise autologous cells on their surface.

49. The kit of claim 18, wherein the microspheres comprise a hydrophilic acrylic copolymer which comprises in copolymerized form about 25% to about 98% of neutral hydrophilic acrylic monomer by weigh, about 2% to about 50% of difunction monomer by weight, and about 0 to about 50% of one or more monomers having a cationic charge.

50. The kit of claim 18, wherein the microspheres further comprise a cell adhesion promoter.

51. The kit of claim 18, wherein the microspheres further comprise autologous cells on their surface.

52. The method of claim 23, wherein the microspheres comprise a hydrophilic acrylic copolymer which comprises in copolymerized form about 25% to about 98% of neutral hydrophilic acrylic monomer by weigh, about 2% to about 50% of difunction

monomer by weight, and about 0 to about 50% of one or more monomers having a cationic charge.

53. The method of claim 23, wherein the microspheres further comprise a cell adhesion promoter.

54. The method of claim 23, wherein the microspheres further comprise autologous cells on their surface.

55. The kit of claim 41, wherein the microspheres comprise a hydrophilic acrylic copolymer which comprises in copolymerized form about 25% to about 98% of neutral hydrophilic acrylic monomer by weigh, about 2% to about 50% of difunction monomer by weight, and about 0 to about 50% of one or more monomers having a cationic charge.

56. The kit of claim 41, wherein the microspheres further comprise a cell adhesion promoter.

57. The kit of claim 41, wherein the microspheres further comprise autologous cells on their surface.

U.S. Patent Application No. 10/220,984, filed 9/9/02 (Our Ref.: 9676-295-999:

1. An injectable composition suitable for tissue construction and generation in a mammal which comprises biocompatible, hydrophilic, non-toxic and substantially spherical microspheres associated with stem cells and a biocompatible carrier, wherein said composition is injectable through needles of about 18 to about 26 gauge and said microspheres are not capable of being displaced, or eliminated by the lymphatic system.

2. The composition of claim1, whercin the stem cells are mesenchymal stem cells isolated from bone marrow, muscle tissues, dermis, or combinations thereof.

3. The composition of claim 1, wherein the microspheres have diameters ranging from about 10 μm to about 500 μm before injection.

4. The composition of claim 3, wherein the microspheres have diameters ranging from about 40 μm to about 300 μm before injection.

5. The composition of claim 4, wherein the microspheres have diameters ranging from about 100 μm to about 300 μm before injection.

6. The composition of claim 1, wherein the composition comprises the microspheres in an amount from about 10% to about 90% by weight and the biocompatible carrier in an amount from about 10% to about 90% by weight.

7. The composition of claim 6, wherein the composition comprises the microspheres in an amount from about 10% to about 50% by weight and the biocompatible carrier in an amount from about 50% to about 90% by weight.

8. The composition of claim 1, wherein the composition is a suspension of said microspheres in said biocompatible carrier.

9. The composition of claim 1, wherein the biocompatible carrier is an emulsion.

10. The composition of claim 1, wherein the biocompatible carrier is organic or non-aqueous solvent.

11. The composition of claim 1, wherein the biocompatible carrier is an aqueous based solution, a hydro-organic solution, or mixtures thereof.

12. The composition of claim 1, wherein the biocompatible carrier is a medium suitable for mesenchymal stem cell culturing.

13. The composition of claim 1, wherein the microspheres swell upon contact with physiological fluids.

14. The composition of claim 1, wherein diameters of the microspheres after injection are about 1 to 4 times of diameters of the microspheres immediately prior to injection.

15. The composition of claim 1, wherein the microspheres comprise one or more elastomers.

16. The composition of claim 15, wherein the elastomers are selected from the group consisting of acrylic polymers, vinyl alcohol polymers, acrylate polymers, polysaccharides, silicones, and mixtures thereof.

17. The composition of claim 1, wherein the microspheres are swellable and comprise polymers selected from the group consisting of sodium acrylate polymer, acrylamide polymer, acrylamide derivative polymer or copolymer, sodium acrylate and vinyl alcohol copolymer, vinyl acetate and acrylic acid ester copolymer, vinyl acetate and methyl maleate copolymer, isobutylene-maleic anhydride crosslinked copolymer, starch-

acrylonitrile graft copolymer, crosslinked sodium polyacrylate polymer, and crosslinked polyethylene oxide.

18. The composition of claim 1, wherein the composition is biodegradable.

19. The composition of claim 1, further comprises therapeutic agent, radio-pacifying agent, contrast medium, or mixtures thereof.

20. The composition of claim 19, wherein said agents or medium are bound to the microspheres.

21. The composition of claim 19, wherein the therapeutic agent is anti-inflammatory agent.

22. The composition of claim 1, wherein the microspheres are capable of being chemically modified to have therapeutic effects, vascularization effects, anti-vascularization effects, visualization properties, anti-inflammatory effects, anti-bacterial effects, anti-histamine effects, or combinations thereof.

23. A method of tissue construction and generation in a mammal comprising administering to said mammal a therapeutically effective amount of a composition of biocompatible, hydrophilic, non-toxic and substantially spherical microspheres associated with stem cells in a biocompatible carrier, wherein the composition is injectable through a needle of about 18 to about 26 gauge and the microspheres are not capable of being displaced, or eliminated by the immune system.

24. The method of claim 23, wherein the stem cells are mesenchymal stem cells isolated from bone marrow, muscle tissues, dermis, or combinations thereof.

25. The method of claim 23, wherein the administration comprises injecting said composition into the mammal.

26. The method of claim 23, wherein the tissue construction and generation is for the treatment of tissue defects in the mammal's heart, coronary vessels, blood vessels, spinal cord, bone, cartilage, tendon, ligament, breast, liver, gallbladder, bile duct, pancreas, intestinal tissues, urinary system, skin, hernia, vocal cord, dental tissues, or combinations thereof.

27. The method of claim 23, wherein the mammal is a human.

28. The method of claim 23, wherein the administration comprises injecting said composition extracorporeally into organs, components of organs, or tissues prior to their inclusion into said mammal's body, organs, or components of organs.

29. The method of claim 23, wherein the composition is injected directly into the site in need of tissue repair.

U.S. Patent Application No. 10/220,982, filed 9/9/02 (Our Ref.: 9676-296-999:

1. A microsphere suitable for active embolization comprising a biocompatible, cross-linked and substantially hydrophilic polymer and one or more active components comprising a drug, a vaccine, or any combination thereof.

2. The microsphere of claim 1, wherein the microsphere comprises one or more elastomers.

3. The microsphere of claim 2, wherein the elastomers are selected from the group consisting of acrylic polymers, acrylamide polymers, vinyl alcohol polymers, acrylate polymers, polysaccharides, silicones, and mixtures thereof.

4. The microsphere of claim 2, wherein the diameter of the microsphere ranges from about 10 μm to about 2000 μm.

5. The microsphere of claim 4, wherein the diameter of the microsphere ranges from about 50 μm to about 300 μm.

6. The microsphere of claim 1, wherein the microsphere is swellable.

7. The microsphere of claim 6, wherein the microsphere comprises polymers selected from the group consisting of sodium acrylate polymer, acrylamide polymer, acrylamide derivative polymer or copolymer, sodium acrylate and vinyl alcohol copolymer, vinyl acetate and acrylic acid ester copolymer, vinyl acetate and methyl maleate copolymer, isobutylene-maleic anhydride crosslinked copolymer, starch-acrylonitrile graft copolymer, crosslinked sodium polyacrylate polymer, and crosslinked polyethylene oxide.

8. The microsphere of claim 6, wherein the diameter of the microsphere ranges from about 10 μm to about 400 μm before swelling.

9. The microsphere of claim 8, wherein the diameter of the microsphere ranges from about 10 μm to about 200 μm before swelling.

10. The microsphere of claim 6, where the diameter of the microsphere ranges from about 10 μm to about 2000 μm after swelling.

11. The microsphere of claim 1, wherein the drug is selected from the group consisting of anti-tumor, anti-angiogenesis, anti-fungal, antiviral, anti-inflammatory drug, anti-bacterial drug, and anti-histamine drug.

12. The microsphere of claim 1, wherein the vaccine is selected from the group consisting of pneumococcus vaccine, poliomyelitis vaccine, anthrax vaccine, tuberculosis (BCG) vaccine, hepatitis A vaccine, cholera vaccine, meningococcus A, C, Y vaccines, W135 vaccine, plague vaccine, rabies (human diploid) vaccine, yellow fever vaccine, Japanese encephalitis vaccine, typhoid (phenol and heat-killed) vaccine, hepatitis B vaccine, diptheria vaccine, tetanus vaccine, pertussis vaccine, *H. influenzae* type b vaccine, polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, varicella vaccine, *streptococcus pneumoniae* Ty (live mutant bacteria) vaccine, Vi (Vi capsular polysaccharide) vaccine, DT (toxoid) vaccine, Td (toxoid) vaccine, aP (inactive bacterial antigen/accelular (DtaP)) vaccine, Hib (bacterial polysaccharide-protein conjugate) vaccine, hepatitis B virus (inactive serum derived viral antigen/recombinant antigen) vaccine, influenza vaccine, rotavirus vaccine, respiratory syncytial virus (RSV) vaccine, human astrovirus vaccine, rotavirus vaccine, human influenza A and B virus vaccine, hepatitis A virus vaccine, live attenuated parainfluenza virus type 3 vaccine, enterovirus vaccines, retrovirus vaccines, and picornavirus vaccines.

13. The microsphere of claim 1, further comprising an imaging agent or contrast media selected from the group consisting of fluorescent markers derivatives, chemical dyes, and magnetic resonance imaging agents.

14. The microsphere of claim 1, wherein the polymer comprises from about 0.5% to about 20%, by molecular weight, of crosslinkers.

15. An injectable composition comprising the microsphere of claim 1 and a biocompatible carrier.

16. The composition of claim 15, wherein the composition comprises the microsphere in an amount from about 10% to about 90% by weight and the biocompatible carrier in an amount from about 10% to about 90% by weight.

17. The composition of claim 16, wherein the composition comprises the microspheres in an amount from about 10% to about 50% by weight and the biocompatible carrier in an amount from about 50% to about 90% by weight.

18. The composition of claim 15, wherein the composition is a suspension of said microspheres in said biocompatible carrier.

19. The composition of claim 18, wherein the biocompatible polymer is in an emulsion.

20. The composition of claim 18, wherein the biocompatible polymer is in an organic or non-aqueous solution.

21. The composition of claim 18, wherein the biocompatible polymer is in an aqueous based solution, a hydro-organic solution, or mixtures thereof.

22. The composition of claim 18, wherein the biocompatible carrier comprises salts composed of cations selected from the group consisting of sodium, potassium, calcium, magnesium, iron, zinc, and ammonium in an amount of from about 0.01 M to about 5 M.

23. The composition of claim 22, wherein the salt is supplied in form of a contrast agent.

24. The composition of claim 18, wherein the contrast agent is monomeric (acrylamido-3-propionamido)-3-triiodo-2,4,6-benzoic acid.

25. The composition of claim 15, where the composition is injectable through a needle of about 18 gauge or smaller.

26. A method for active embolization in a mammal comprising administering to a mammal in need of treatment a microsphere comprising a biocompatible, cross-linked and substantially hydrophilic polymer and one or more drugs, vaccines, or combinations thereof.

27. The method of claim 26, wherein the microsphere comprises one or more elastomers.

28. The method of claim 27, wherein the elastomers are selected from the group consisting of acrylic polymers, acrylamide polymers, vinyl alcohol polymers, acrylate polymers, polysaccharides, silicones, and mixtures thereof.

29. The method of claim 27, wherein diameter of the microsphere ranges from about 10 μm to about 2000 μm.

30. The method of claim 29, wherein the diameter of the microsphere ranges from about 50 μm to about 300 μm.

31. The method of claim 26, wherein the microsphere is swellable.

32. The method of claim 31, wherein the microsphere comprises ionic polysaccharides and ionic synthetic polymers.

33. The method of claim 32, wherein the ionic polysaccharides are selected from the group consisting of carboxymethyldextran, dextran sulphate, and algenic acid.

34. The method of claim 32, wherein the ionic synthetic polymers are selected from the group consisting of sodium acrylate polymer, acrylamide polymer, acrylamide derivative polymer or copolymer, sodium acrylate and vinyl alcohol copolymer, vinyl acetate and acrylic acid ester copolymer, vinyl acetate and methyl maleate copolymer, isobutylene-maleic anhydride crosslinked copolymer, starch-acrylonitrile graft copolymer, crosslinked sodium polyacrylate polymer, and crosslinked polyethylene oxide.

35. The method of claim 31, wherein diameter of the microsphere ranges from about 10 μm to about 400 μm before swelling.

36. The method of claim 35, wherein the diameter of the microsphere ranges from about 10 μm to about 200 μm before swelling.

37. The method of claim 31, where diameter of the microsphere ranges from about 10 μm to about 2000 μm after swelling.

38. The method of claim 26, wherein the therapeutically active drug is selected from the group consisting of anti-tumor, anti-angiogenesis, anti-fungal, antiviral, anti-inflammatory drug, anti-bacterial drug, and anti-histamine drug, anti-angiogenic factor, antineoplastic agents, hormones and steroids, vitamins, peptides and peptide analogs, enzymes, anti-allergenic agents, circulatory drugs, anti-tubercular agents, anti-viral agents, anti-anginal agents, anti-protozoan agents, anti-rheumatic agents, narcotics, cardiac glycoside agents, sedatives, local anesthetic agents, general anesthetic agents.

39. The method of claim 26, wherein the vaccine is selected from the group consisting of pneumococcus vaccine, poliomyelitis vaccine, anthrax vaccine, tuberculosis (BCG) vaccine, hepatitis A vaccine, cholera vaccine, meningococcus A, C, Y vaccines, W135 vaccine, plague vaccine, rabies (human diploid) vaccine, yellow fever vaccine,

Japanese encephalitis vaccine, typhoid (phenol and heat-killed) vaccine, hepatitis B vaccine, diptheria vaccine, tetanus vaccine, pertussis vaccine, *H. influenzae* type b vaccine, polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, varicella vaccine, *streptococcus pneumoniae* Ty (live mutant bacteria) vaccine, Vi (Vi capsular polysaccharide) vaccine, DT (toxoid) vaccine, Td (toxoid) vaccine, aP (inactive bacterial antigen/accelular (DtaP)) vaccine, Hib (bacterial polysaccharide-protein conjugate) vaccine, hepatitis B virus (inactive serum derived viral antigen/recombinant antigen) vaccine, influenza vaccine, rotavirus vaccine, respiratory syncytial virus (RSV) vaccine, human astrovirus vaccine, rotavirus vaccine, human influenza A and B virus vaccine, hepatitis A virus vaccine, live attenuated parainfluenza virus type 3 vaccine, enterovirus vaccines, retrovirus vaccines, and picornavirus vaccines.

40. The method of claim 26, wherein the microsphere further comprises a contrast media or a diagnostic agent selected from the group consisting of fluorescent markers derivatives, chemical dyes, and magnetic resonance imaging agents.

41. The method of claim 26, wherein the polymer comprises from about 0.5% to about 20%, by molecular weight, of crosslinkers.

42. The method of claim 26, wherein the administration comprises injecting into an area of said mammal in need of embolization.

43. The microsphere of claim 1, wherein the anti-tumor drug is taxol, doxorubicin, tamoxifen, or a combination thereof.

44. A method for active embolization in a mammal comprising administering to a mammal in need of treatment a microsphere comprising a biocompatible, cross-linked and substantially hydrophilic polymer and one or more drugs, vaccines, or combinations thereof, wherein said microsphere is delivered to the site of action by the use of targeting antibodies.

U.S. Patent Application No. 10/029,294, filed 12/28/01(Our Ref.: 9676-311-999):

1. A method for treating gastroesophageal reflux disease, which comprises administering to a mammal in need of such treatment a therapeutically effective tissue bulking amount of biocompatible hydrophilic microparticles, said administration being into the lower esophageal sphincter or the diaphragm.

2. The method of claim 1, wherein the microparticles are cationic.

3. The method of claim 1, wherein the microparticles comprise a positive charge on their surface.

4. The method of claim 1, wherein said mammal is a human.

5. The method of claim 1, wherein the microparticles are pre-treated with, administered with, or coated with autologous cells.

6. The method of claim 5, wherein the microparticles or cell coated microparticles are washed with serum or whole blood prior to administration.

7. The method of claim 5, wherein the autologous cells are mucosal cells, muscle cells, fat cells, or combinations thereof.

8. The method of claim 1, wherein the microparticles are coated with or linked to at least one collagen or a derivative thereof, glucosaminoglycans, or a mixture thereof.

9, The method of claim 1, wherein the microparticles are administered in a sterile and pyrogen-free injectable solution.

10. The method of claim 1, wherein the microparticles are spherical.

11. The method of claim 10, wherein the microparticles comprise a hydrophilic copolymer which comprises in copolymerized form about 25 to about 99% by weight of neutral hydrophilic acrylic monomer, about 2 to about 50% by weight of one or more monomers having a cationic charge, and about 1 to about 30% by weight of a functionalized monomer.

12. The method of claim 10, wherein said microparticles have diameters ranging from about 10μm to about 1000μm.

13. The method of claim 1, wherein said administration is made via syringe, catheter, or combinations thereof.

14. The method of claim 1, wherein said microparticles comprise or are administered with one or more of a therapeutic agent, an anti-inflammatory agent, an angiogenesis inhibitor, a radio active element, and an antimitotic agent.

15. The method of claim 1, wherein the microparticles further comprise a cell adhesion promoter.

16. The method of claim 15, wherein said cell adhesion promoter is selected from the group consisting of fibronectin, laminin, chondronectin, entacin, epibolin, liver cell adhesion molecule, serum spreading factor, collagen, heparin sulfates, dermatan sulfates, chonodroctin sulfates, glucosaminoglycans, and mixtures thereof.

19. A method for treating gastroesophageal reflux disease, which comprises:
(a) preparing cationic microparticles which comprise biocompatible and hydrophilic polymers;
(b) administering the resulting microparticles to a mammal by injection into walls of a sphincter located where the esophagus meets the stomach.

20. The method of claim 19, wherein the microparticles further comprise a cell adhesion promoter.

U.S. Patent Application No. 10/222,819, filed 8/19/02 (Our Ref.: 9676-312-999):

1. An injectable composition suitable for dermal augmentation in a mammal which comprises biocompatible, swellable, hydrophilic, non-toxic and substantially spherical microspheres and a biocompatible carrier, wherein said composition is injectable through needles of about 30 gauge or smaller and wherein said microspheres swell to a predetermined size after injection.

2. The composition of claim 1, wherein the composition comprises the microspheres in an amount from about 10% to about 90% by weight and the biocompatible carrier in an amount from about 10% to about 90% by weight.

3. The composition of claim 2, wherein the composition comprises the microspheres in an amount from about 10% to about 50% by weight and the biocompatible carrier in an amount from about 50% to about 90% by weight.

4. The composition of claim 1, wherein the composition is a suspension of said microspheres in said biocompatible carrier.

5. The composition of claim 4, wherein the biocompatible carrier is an emulsion.

6. The composition of claim 4, wherein the biocompatible carrier is an organic or non-aqueous solution.

7. The composition of claim 4, wherein the biocompatible carrier is an aqueous based solution, a hydro-organic solution, or mixtures thereof.

8. The composition of claim 4, wherein the biocompatible carrier comprises salts composed of cations selected from the group consisting of sodium, potassium, calcium, magnesium, iron, zinc, and ammonium in an amount of from about 0.01 M to about 5 M.

9. The composition of claim 8, wherein the salt is supplied in form of a contrast agent.

10. The composition of claim 4, wherein the biocompatible carrier is acylamino-e-propion-amido-3-triiodo-2, 4, 6-benzoic acid.

11. The composition of claim 1, wherein average diameters of the microspheres after injection are about 1 to 4 times of average diameters of the microspheres immediately prior to injection.

12. The composition of claim 1, wherein there is no aggregation or clumping of the microspheres prior to and during injection.

13. The composition of claim 1, wherein the microspheres comprise sodium acrylate polymer, acrylamide polymer, acrylamide derivative polymer or copolymer, sodium acrylate and vinyl alcohol copolymer, vinyl acetate and acrylic acid ester copolymer, vinyl

acetate and methyl maleate copolymer, isobutylene-maleic anhydride crosslinked copolymer, starch-acrylonitrile graft copolymer, crosslinked sodium polyacrylate polymer, crosslinked polyethylene oxide, or mixtures thereof.

14. The composition of claim 13, wherein the polymers comprise from about 0.5% to about 20%, by molecular weight, of crosslinkers.

15. The composition of claim 1, which further comprises cells associated with surfaces of at least a portion of the microspheres prior to injection.

16. The composition of claim 15, wherein the cells are autologous cells from the subject mammal.

17. The composition of claim 16, wherein the autologous cells are fat cells, muscle cells, subcutaneous cells, dermal cells, epidermal cells, or combinations thereof.

18. The composition of claim 1, further comprises therapeutic agent, radio-pacifying agent, contrast medium, or mixtures thereof.

19. The composition of claim 18, wherein said agents or medium are bound to the microspheres.

20. The composition of claim 18, wherein the therapeutic agent is anti-inflammatory agent.

21. The composition of claim 1, wherein the microspheres are capable of being chemically modified to have therapeutic effects, anti-inflammatory effects, anti-bacterial effects, anti-histamine effects, or combinations thereof.

22. A method of dermal augmentation in a mammal comprising injecting a composition comprising biocompatible, swellable, hydrophilic, non-toxic and substantially spherical microspheres in a biocompatible carrier to said mammal through a needle of about 30 gauge or smaller.

23. The method of claim 22, wherein the composition is a suspension of said microspheres in said biocompatible carrier.

24. The method of claim 22, wherein the microspheres swell upon contacting with physiological fluids at injection site.

25. The method of claim 24, wherein diameters of the microspheres after injection are about 1 to about 4 times of diameters of the microspheres immediately prior to injection.

26. The method of claim 22, wherein the microspheres comprise sodium acrylate polymer, acrylamide polymer, acrylamide derivative polymer or copolymer, sodium acrylate and vinyl alcohol copolymer, vinyl acetate and acrylic acid ester copolymer, vinyl acetate and methyl maleate copolymer, isobutylene-maleic anhydride crosslinked copolymer, starch-

acrylonitrile graft copolymer, crosslinked sodium polyacrylate polymer, crosslinked polyethylene oxide, or mixtures thereof.

27. The method of claim 22, which further comprises cells associated with surfaces of at least a portion of the microspheres prior to administration.

28. The method of claim 27, wherein the cells are autologous cells from the subject mammal.

29. The method of claim 28, wherein the autologous cells are fat cells, muscle cells, subcutaneous cells, dermal cells, epidermal cells, or combinations thereof.

30. The method of claim 23, wherein the biocompatible carrier is an emulsion.

31. The method of claim 23, wherein the biocompatible carrier is organic or non-aqueous solvent.

32. The method of claim 23, wherein the biocompatible carrier is an aqueous solution, a hydro-organic solution, or mixtures thereof.

33. The method of claim 23, wherein the biocompatible carrier comprises salts composed of cations selected from the group consisting of sodium, potassium, calcium, magnesium, iron, zinc, and ammonium in an amount of from about 0.01 M to about 5 M.

34. The method of claim 23, wherein the salt is supplied in form of a contrast agent.

35. The method of claim 23, wherein biocompatible solvent is acylamino-e-propion-amido-3-triiodo-2, 4, 6-benzoic acid.

36. The method of claim 22, wherein the composition further comprises therapeutic agent, radio-pacifying agent, contrast media, or mixtures thereof.

37. The method of claim 36, wherein said therapeutic agents are bound to the microspheres.

38. The method of claim 22, wherein the microspheres are capable of being chemically modified to have therapeutic effects, anti-inflammatory effects, anti-bacterial effects, anti-histamine effects, or combinations thereof.

39. The method of claim 38, wherein the chemical modification of the microspheres are caused by interactions between the microspheres and neighboring tissues after injection thereof.

40. The method of claim 22, wherein the injection is into an area of said mammal in need of dermal augmentation.

41. The method of claim 40, wherein the administration comprises injecting said composition into the subcutaneous layer.

42. The method of claim 22, wherein the dermal augmentation is for treatment of contour deficiencies of said mammal.

43. The method of claim 42, wherein the contour deficiencies are caused by aging, environmental exposure, weight loss, child bearing, surgery, disease or combinations thereof.

44. The method of claim 42, wherein the contour deficiencies are one or more of the group consisting of frown lines, worry lines, wrinkles, crow's feet, marionette lines, stretch marks, and internal and external scars resulted from injury, wound, bite, or surgery.

45. The method of claim 43, wherein the disease is acne, cancer, or combination thereof.

46. The method of claim 22, wherein the mammal is human.

47. The method of claim 22, wherein the administration comprises injecting said composition extracorporeally into organs, components of organs, or tissues prior to their inclusion into said mammal's body, organs, or components of organs.

48. A kit for performing dermal augmentation comprising:

(a) a 30 gauge or smaller needle;

(b) means for injecting a liquid based composition through said needle; and

(c) biocompatible, swellable, crosslinked, hydrophilic, non-toxic and substantially spherical microspheres injectable through said needle and are not capable of being digested or eliminated by macrophage or other elements of said mammal's immune system after injection thereof.

49. The kit of claim 48, wherein the means for injection is a syringe corresponding to said needle.

50. The kit of claim 48, further comprising a liquid based biocompatible carrier injectable through said needle.

51. The kit of claim 50, wherein the microspheres are suspended in the biocompatible carrier.

52. The kit of claim 51, wherein the microspheres are associated with cells.